Public Workshop

Complex Issues in Developing Drug and Biological Products for Rare Diseases

FDA White Oak Campus (Silver Spring, MD)
January 6-7, 2014

AGENDA - DAY 1

January 6, 2014

"Complex Issues in Rare Disease Drug Development"

8:00-8:10 am **Welcome, General Scope and Objectives of the Workshop**

Anne Pariser, M.D., Associate Director for Rare Diseases, Office of New Drugs (OND), Center for Drug Evaluation and Research (CDER), FDA

8:10-8:30 am **Keynote Address: State of Rare Disease Drug Development**

Speaker: Richard Moscicki, M.D., Deputy Center Director for Science Operations, CDER, FDA

8:30-8:45 am **Introduction – Overview of Day 1**

Anne Pariser, M.D., Associate Director for Rare Diseases, CDER OND, FDA

8:45-10:15 am **Session 1: Complex Issues for Trial Design: Endpoints**

Session Chair: Edward Cox, M.D., M.P.H., Director, Office of Antimicrobial Products, OND CDER, FDA

Discussion topics:

- Discuss the role of information on the natural history of disease, effects of treatment, and patient benefits, in development of endpoints for clinical trials.
- Discuss possible sources of information to characterize the natural history of disease and the effects of treatment.
- Discuss what mechanisms and approaches could be utilized to facilitate endpoint development.
- Discuss ways in which endpoint development efforts might be organized.

Session breakdown

- Chair presentation – Overview of subtopics & background for the session (10 min)
- Panel discussion

- Summary (5 min)

10:15-10:30 am **Break**

10:30 am-12:00 pm **Session 2: Complex Issues for Trial Design: Study Design, Conduct and Analysis**

Session Chair: Ellis Unger, M.D., Director, Office of Drug Evaluation I, OND CDER, FDA

Discussion topics:

- Alternative study designs
- More efficient dose selection
- Enrichment strategies
- Benefit-risk considerations

Session breakdown

- Chair presentation (10 min)
- Panel discussion
- Summary (5 min)

12:00-1:00 pm **Lunch** (on your own)

1:00-2:30 pm **Session 3: Foundational Science**

Session Chair: Marc Walton, M.D. Ph.D., Associate Director for Translational Medicine, Office of Translational Sciences, CDER, FDA

Discussion topics:

- Natural History of Rare Diseases
  - Discuss the role of natural history knowledge in rare disease drug development and the models for obtaining this knowledge.
- Animal Models of Disease
  - Discuss the importance and limitations of animal models of a disease in drug development and how we determine how useful any particular animal model may be.
- Biomarkers of Pathophysiologic Processes
  - Discuss where in the process of drug discovery and drug development biomarkers can play an important role, what impact of those roles are, what characteristics of biomarkers may make them more or less well suited for the different roles in general or in different categories of disorders.
- Resources for foundational science
  - Where might resources for these or other foundational science activities be found?

Session breakdown

- Chair presentation (10 min)
- Panel discussion
- Summary (5 min)

2:30-2:45 pm **Break**

2:45-4:15 pm **Session 4: Safety and Dosing**

Session Chair: Mwango Kashoki, M.D., M.P.H., Associate Director for Safety, OND CDER, FDA

Discussion topics:

- Drug development
  - Assessing safety in small trials – exposure, numbers and duration

- Post-marketing safety considerations
  - Pharmacovigilance strategies
  - Registries (to collect additional drug safety data)
  - Risk management/REMS with elements to assure safe use (ETASU)
  - Risk tolerance

Session breakdown

- Chair presentation (10 min)
- Panel discussion
- Summary (5 min)

4:15-5:00 pm **Session 5: Day 1 Summary**

Anne Pariser, M.D., Associate Director for Rare Diseases, CDER OND, FDA

- Summarize main ideas from Day 1 discussions
- Panel discussion
- Closing statement and path forward

5:00 pm **Adjourn**

AGENDA - DAY 2

January 7, 2014

"Encouraging and Accelerating Development of New Therapies for Pediatric Rare Diseases"

8:00-8:20 am **Introduction to Pediatric Issues**

Dianne Murphy, M.D., F.A.A.P., Director, Office of Pediatric Therapeutics (OPT), Office of the Commissioner (OC), FDA

8:20-9:50 am **Session 6: Networks and Collaborations in Support of Pediatric Clinical Trials**

Session Chair: Anne Zajicek, M.D**.,** Pharm.D., National Institute of Child Health and Development, NIH

- *Panel discussion followed by audience participation*

Discussion topics:

- Elements (good and bad) of clinical trials network for pediatric drug/device approval
- Examples of model networks
- Legislation in EU mandates establishing peds networks: effect on pediatric networks in the US
- What does it take to get a peds trial up and running
  - Management infrastructure
  - Protocol with achievable endpoints
  - Clinical investigators capable of enrolling, performing clinical trial
  - Clinical trial materials
  - Patients
  - Data Monitoring Committee
- Role of advocacy groups
  - Encouraging research, development of new therapeutics
  - Definition of meaningful clinical benefit
  - Patient availability
- How to accelerate pivotal clinical trials of new drugs, e.g., through the use of response biomarkers and other surrogate endpoints

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9:50-10:05 am **Break**

10:05-11:35 am **Session 7: Tolerating Risk and Uncertainty in Pediatric Clinical Trials**

Session Chair: Robert (Skip) Nelson, M.D., Ph.D., Deputy Director and Senior Pediatric Ethicist, OPT, OC, FDA

- *Panel discussion followed by audience participation*

Discussion topics:

- Context: Life-threatening pediatric disease for which there are limited to no alternative treatments
- Discuss the risks that may be justified given the potential for clinical benefit, given limitations of data from non-clinical disease models and adult human experience
- Types of harms we are willing to risk given the severity and progression of a child's disease
- The level of tolerable uncertainty about the probability of those harms

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11:35 am-12:30 pm **Lunch** (on your own)

12:30-2:00 pm **Session 8: Pediatric Oncology**

Session Chair: Gregory Reaman, M.D., Associate Director, Office of Hematology and Oncology Products, OND, CDER, FDA

- *Panel discussion followed by audience participation*

Discussion topics:

- Define "meaningful" clinical benefit for children with life-threatening diseases: aligning perspectives of patients, families, providers, industry, and regulators
- Address the current "indication-driven" mandate (PREA) for new drug evaluation for pediatric cancers vs. mechanism of action, antigen targets, and pathway inhibition,
- How to accelerate pivotal clinical trials of new drugs in pediatric cancers, e.g., through the use of response biomarkers as surrogate endpoints and other supporting data
- Address the various perspectives around the concept of "risk" in pediatric cancer clinical research and drug development: Individual and population safety vs. program development.
- Address the perceived barriers to new drug development in pediatric cancer due to procedural and programmatic differences between international regulatory agencies

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2:00-2:15 pm **Break**

2:15-3:45 pm **Session 9: Gene Therapy Trials in Pediatric Patients**

Session Chair: Ilan Irony, M.D., Branch Chief, Office of Cellular, Tissue and Gene Therapies, Center for Biologics Evaluation and Research (CBER), FDA

- *Panel discussion followed by audience participation*

Discussion topics:

- Development of interventions with long-acting / permanent effects
- Development of products by individual researchers / academicians, or small pharmaceutical companies, rather than large companies
- Development considerations for invasive procedures that may be used to delivery gene therapies (e.g., to heart or brain)
- Product modifications (e.g., changes in vector, promoter, or transgene) for treatment of rare diseases
- Objectives of early-phase trials (e.g., feasibility in manufacturing, investigator training, goals of dose escalation)

3:45-4:45 pm **Session 10: Day 2 Summary**

Dianne Murphy, M.D., F.A.A.P., Director, OPT, OC, FDA

4:45 pm **Adjourn**